REMARKS

Claims 13-17 are currently pending. Support for amendments to Claim 13 can be found in the Specification as filed, for example at paragraphs [0024], [0025], [0073], [0075], and [0078]. Therefore, the amendments do not result in a subject matter that goes beyond the original disclosure. The following addresses the substance of the Office Action.

Obviousness

Claims 13, 14, 15 and 20 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Masaru et al. (European Patent Application EP 0728469 A2, published August 18, 1996) as evidenced by CRC Press (Definitions, Conversions, and Calculations for Occupational Safety and Health Professionals, Third Edition, 2006, pp. 8-3 to 8-7).

The subject matter of Masaru et al. relates to an endermic liniment which has a melanin production suppressing effect and is superior in terms of its skin whitening effect such as preventing and/or improving chloasma, freckles and pigmentation in the skin after sunburn (Masaru et al., abstract). According to the authors of Masaru et al., the development of chloasma, freckles and pigmentation after sunburn is caused by the formation of melanin pigment, e.g., due to ultraviolet light stimulation from sunlight followed by abnormal deposition of this pigment in the skin; (See Masaru et al., page 2, lines 11 to 13). It was the intention of the authors to find a compound that suppresses the production of melanin, and has a whitening effect on the skin that is superior to hydroquinone, currently used in the art for that purpose (Masaru et al., page 2, lines 13 to 17, and lines 25 to 27).

The authors performed several experiments, designated as "Whitening Effect Tests 1 to 3," as described on pages 7-11 of Masaru et al. In "Whitening Effect Test 1" the authors treated Weiser Maple guinea pigs, having phototoxic pigmentation, with several drugs applied on an approximately 4 cm^2 area on the shaved back of these animals. The investigators analyzed whether decoloration of the pigmentation or enhancement of pigmentation occurred after 8 weeks of a daily application of such drugs (see Masaru et al., page 7, lines 24 to 33). The drugs tested are listed in Table 1 on page 8. Five different phenylalanine derivatives were tested, namely N-benzyloxycarbonyl-L-tyrosine DL-O-tyrosine, O-benzyl-L-tyrosine, N-acetyl-L-tyrosine amide, and L-tyrosine amide hydrochloride.

In the "Whitening Effect Test 2," ninety subjects were treated twice a day with the drugs listed above on their skin for a time period of 8 weeks and exposed to summer sun light. The degree of the decrease of pigmentation was assessed (see Masaru et al., page 9, lines 25 to 55.

Finally, in the "Whitening Effect Test 3," the authors treated patients suffering from dark skin, chloasma, freckles for a time period of three months by daily administering the drugs as identified above. The authors analyzed whether the pigmentation had decreased.

Masaru et al. did not test any phosphate-containing phenylalanine derivatives, let alone phosphotyrosine. The only mention of phosphotyrosine in the reference is on page 3, lines 16-17 and 21-22, wherein phosphotyrosines are listed along with a large number of other phenylalanine derivatives. However, there is no experimental evidence that such compounds have any effect on improving pigmentation after sunburn. Since the authors of Masaru et al. did not even perform a single experiment using a phosphorylated compound, a person skilled in the art would not consider such compounds as having a skin whitening effect or any effect. Indeed, Masaru et al. does not teach that phosphorylation, *per se,* can be used to prevent skin damage caused by exposure to UV-light. The only conclusion that can be drawn from Masaru et al. is that the substances as identified on page 8 (Table 1) and in Examples 1 to 5 can be used to whiten the skin as in the case of cloasma freckles, or to prevent skin darkening upon sun exposure effected by an increased formation of melanin pigment and pigmentation after sunburn.

The subject matter of amended Claim 13 is directed to a method for specifically protecting non-transformed biological cells over transformed biological cells from cell damage induced by radiation, ultraviolet light, and chemicals. The inventors pre-treated normal human skin fibroblasts (HSF6 and HSF1) and transformed human skin fibroblasts comprising a mutation in the p53 gene (HH4dd). These cells were then exposed to radioactivity (Examples 4 and 6), UV-B irradiation (Example 7), or cisplatin (Example 8). In all three cases, the inventors realized that phosphotyrosine has a clear protective effect on normal human skin fibroblasts (HSF6 and HSF1). In contrast, a protective effect was not observed with regard to transformed human skin fibroblasts (HH4dd). To the contrary, the toxicity of the cell damaging factors on the transformed human skin fibroblasts (HH4dd) was increased after the pretreatment with phosphotyrosine as exemplified by the cell damaging factors of radioactivity or ionizing radiation, respectively (paragraph [0073] and Fig. 2b of the Specification as filed) and cisplatin

(Fig. 6b). Thus, the inventors have demonstrated for the very first time that the administration of phosphotyrosine on biological material can selectively protect non-transformed biological cells whereas transformed biological cells are not protected from cell damaging factors.

Claim 16 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Ramsay et al. (1992 *Arch Derm* **128**, No. 7; Abstract) in view of Masaru et al. (*supra*). Ramsay et al. describes a protective role for UV-B irradiation on patients affected by cutaneous T-cell lymphoma (CTCL). In other words, this document relates to UV-B irradiation as a phototherapy for early stage CTCL. As such, the Ramsay reference is not relevant to the subject matter of the present application, which uses phosphotyrosine to selectively protect non-transformed biological cells over transformed biological cells. Thus, the combination of Ramsay et al. and Masaru et al. does not support a case of *a priori* obviousness since neither reference provides any reason to one of skill in the art to use phosphotyrosine to selectively protect non-transformed biological cells over transformed biological cells.

Neither document Masaru et al. or Ramsay et al., nor a combination thereof renders obvious the presently claimed method for selectively protecting non-transformed biological cells over transformed biological cells. Masaru et al. discloses a method for suppressing the pigmentation, or of promoting the whitening of skin by the use of N-benzyloxycarbonyl-L-tyrosine DL-O-tyrosine, O-benzyl-L-tyrosine, N-acetyl-L-tyrosine amide, and L-tyrosine amide hydrochloride. Ramsay et al. discloses a. method for treating cutaneous T-cell lymphoma by the administration of UV-B irradiation. Thus, the skilled person would not obtain any helpful information from these documents with regard to selectively protecting non-transformed biological cells over transformed biological cells.

In view of the amendments to the claims and the foregoing remarks, the Applicants believe the subject matter of amended Claim 13 to be in compliance with the requirements of 35 U.S.C. § 103(a) and withdrawal of the rejection is respectfully requested.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

It is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 10, 2008

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